DETAILED ACTION

Acknowledgement is made to Applicant's response filed 04/04/2011.

Claims 2-5, 11, 15, 18-33 and 35-40 are pending.

Claims 1-5 and 18-23 were previously withdrawn.

Claims 2-5 have been rejoined in view of Applicant's amendments to said claims.

Claims 2-5, 11, and 15 are currently amended.

Claims 39 and 40 are newly added.

Claims 2-5, 11, 15, 24-33, and 35-40 are currently under consideration.

Withdrawn Rejections

The rejection of claims 11, 14, 15, 24-27, 29, 30, and 34 under 35 U.S.C. 102(b) as being anticipated by Martin et al (U.S. Patent number 5,602,183, Patent issued Feb. 11, 1997) as evidenced by the specification is withdrawn in view of Applicant's amendments to no longer pursue pyruvate as a 2–oxoacid or the patient population of those "in need of neovascularization", those "suffering from thrombosis", or "in need of wound or burn healing".

The rejection of claims 11, 14, 15, 24-31, and 33-38 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification is withdrawn in view of Applicant's amendments

to no longer pursue pyruvate as a 2–oxoacid or the patient population of those "in need of neovascularization" or "in need of wound or burn healing".

Claims 11, 13-15, 24-31, and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification as applied to claims 11, 14, 15, 24-31, and 33-38 above, and further in view of Fujii et al (2002, European Journal of Cardio-Thoracic Surgery) is withdrawn in view of Applicant's amendments to no longer pursue pyruvate as a 2–oxoacid or the patient population of those "in need of neovascularization", those "suffering from thrombosis", or "in need of wound or burn healing".

The rejection of claims 11, 14, 15, and 24-38 under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification as applied to claims 11, 14, 15, 24-31, 33-38 above, and further in view of Dykstra (U.S. PreGrant Publication number 2003/0212134) is withdrawn in view of Applicant's amendments to no longer pursue pyruvate as a 2–oxoacid or the patient population of those "in need of neovascularization", those "suffering from thrombosis", or "in need of wound or burn healing".

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5, 11, 15, 24-33, and 35-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed 04/04/2011 has introduced NEW MATTER into the claims.

As presently amended claim 11 recites that the composition consists of at least one 2-oxoacid from those listed "and at least one or more pharmaceutically acceptable excipients or food additives". Thus, the claim broadly encompasses the addition of any and all pharmaceutically acceptable excipients and food additives, in particular food additives were not previously encompassed by the claims or the specification as originally filed.

The response did not point out where support for currently amended claim 11 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure.").

As presently amended, the claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the presently amended claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

It is noted that while it would have been obvious to utilize certain excipients, obviousness is not the standard for the addition new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed. *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961 (Fed. Cir. 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-5, 11, 14, 15, 24-31, 33, and 35-40 are rejected under 35 U.S.C. 103(a) as obvious over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification in view of Guezennec et al (Int. J. Sports Med.).

Teichberg teaches a method of reducing extracellular brain glutamate levels by delivering a therapeutic amount of an active (see Abstract). Said composition comprises an active agent that is taught as being selected from oxaloacetate diethylester, oxaloacetate, pyruvate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate (see entire document, for instance [0025]), this reads on **instant claims 11 and 34-38**. Teichberg teaches that the preferred subjects of said method are canines, felines, ovines, porcines, equines, bovines, and humans (see entire document,

for instance [0102]), this reads on the limitation of "human subject" in **instant claim 11**. Teichberg teaches that the composition can be applied topically (see entire document, for instance [0126] and [0134]), this reads on **instant claim 15**. Teichberg also teaches that the composition can be administered rectally via enemas (see entire document, for instance [0146]), by the nasal route via a spray (see entire document, for instance [0142]), orally via a capsule (see entire document, for instance [0140]), ocularly via intraocular injection, which would encompass solutions and suspensions (see entire document, for instance [0133] and [0144]), and subcutaneously via an injection of a pharmaceutical composition which comprises a carrier (see entire document, for instance [0133] and 0127]), these read on **instant claims 24-26, and 27, 28, 29, 30, and 31, respectively**. Teichberg identifies that the composition comprises lipophilic solvents or vehicles such as fatty oils when the composition is being administered parenterally (see entire document, for instance [0144]). Teichberg identifies that in certain scenarios, for instance, in brain surgery, the composition is applied topically (see [0126]). Teichberg also teaches that the composition can be administered in a plurality of administrations over several days or weeks and that a skilled artisan would be able to vary the amount in order to meet the specific needs of the scenario (see [0152] and [0153]), this reads on **instant claim 33**. Furthermore, Teichberg teaches that the composition can comprise pharmaceutically acceptable excipients (see entire document, for instance, [0128]).

Teichberg, while teaching reducing glutamate levels, fails to directly identify those patient population includes those suffering from acute hypoxia (independent

instant claim 11), and particularly acute hypoxia caused by exercise (newly added claim 39).

Guezennec tests to see the effects of prolonged exercise on brain amino acid (glutamate) levels (see entire document, for instance, Title). Guezennec teaches that "brain glutamine was increased at exhaustion in all groups of running rats by 30-75%" (see entire document, for instance, page 323, column 1, first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the composition of Teichberg for patients who have just exercised. One would have been motivated to do so since Guezennec teaches that exercise induces increased glutamate levels, and Tiechberg teaches that the composition of Tiechberg reduces excess glutamate levels. There would be a reasonable expectation that the composition of Teichberg would reduce the glutamate levels in patients who have exercised since Teichberg directly teaches the reduction in glutamate levels by using the composition of Teichberg.

With regard to the inducing of HIF-1 mediated gene expression, as evidenced by the specification "the endogenous 2-oxoacids pyruvate and oxaloacetate compete for the 2-oxoglutarate binding site in HIF hydroxylating enzymes and then lead to their inactivation. This results in long-lasting HIF-1α accumulation and activation of HIF-1α mediated gene expression, even in the presence of oxygen" (see instant specification, page 14, first paragraph). Therefore, the method of Teichberg, which teaches the administration of, for example, oxaloacetate, would necessarily induce HIF-1 mediated gene expression. Merely discovering and claiming a new benefit of an *old* process

cannot render the process again patentable. *Verdegaal Bros., Inc. v. Union Oil Co. of Calif.,* 814 F.2d 628, 632-33, 2USPQ2d 1051, 1054 (Fed. Cir.), cert. Denied, 484 U.S. 827 (1987). *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990), which states "a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable."

With regard to the active utilized, it would have been obvious to one of ordinary skill in the art would utilize any one of oxaloacetate, pyruvate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate as the active in the composition of Teichberg. One would have been motivated to do so since Teichberg teaches said actives in a short list of preferred active ingredients in paragraph [0025]. There would be a reasonable expectation of success in the use of said active since they are directly taught by Teichberg.

With regard to the method of utilizing the composition being directed to promoting tissue vascularization in skeletal muscle tissue, it has been established that the composition taught by Teichberg is to be utilized on patients who have excessive glutamate levels, wherein Guezennec teaches that exercise causes excess glutamate levels. Furthermore, the patient population in Teichberg, once their glutamate levels are decreased, would necessarily show increased HIF-1 expression. This is evidenced by the instant specification (for instance, page 14, first paragraph), and Semenza evidencing that accumulation of HIF results in neovascularization (see Semenza, entire document, for instance, Abstract). Hence, since the administration of the composition of Teichberg would necessarily induce HIF-1 mediated gene expression, there would also

necessarily be vascularization of skeletal muscle occurring in the patient with whom the composition of Teichberg is being administered.

Response to Arguments

Applicant argues in the response filed 04/04/2011 that "Teichberg does not disclose or suggest the use of any 2-oxoacid for increasing tissue vascularization in muscle tissue as set forth in the amended claims" (see remarks, page 6). Applicant's argument is not found persuasive with regard to the new grounds of rejection since the teachings of Teichberg in view of Guezennec, as set forth above, would result in the same composition (2-oxoacid), being provided to the same population (patients who have exercised, and therefore have increased glutamate levels), in the amount required by the claims (an amount). Therefore, the composition of Teichberg in view of Guezennec would result in increasing tissue vascularization in muscle tissue. It is noted that MPEP 2112 states: "Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." It is further noted that the art is not required to teach the same reasoning for adding components as Applicant, MPEP 2144 (IV) states "the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicant. See, e.g., In re Kahn, 411 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)."

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Semenza (2001, Pediatric Research) and the instant specification in view of Guezennec et al (Int. J. Sports Med.) as applied to claims 2-5, 11, 14, 15, 24-31, 33, and 35-40 above, and further in view of Dykstra (U.S. PreGrant Publication number 2003/0212134).

The teachings of Teichberg, Semenza, the instant specification, and Guezennec are set forth above, wherein it is again noted that Teichberg identifies that the composition comprises lipophilic solvents or vehicles such as fatty oils (see entire document, for instance [0144]).

Teichberg, while teaching topical delivery, fails to directly identify that the composition is in transdermal form.

Dykstra teaches that "[f]or transdermal administration, the active ingredients may be conveniently incorporated into a lipophilic carrier and formulated as a topical crème or adhesive patch" (see entire document, for instance, [0024]). It is further noted that Dykstra teaches pyruvate derivatives as preferred actives (see entire document, for instance, [0009]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the composition of Teichberg as a transdermal patch. One would have been motivated to do so since transdermal delivery is a well known method of drug delivery. There would have been a reasonable expectation of success since Teichberg teaches that the composition can comprise lipophilic vehicles, wherein

Dykstra teaches that transdermal patches and topical creams are made by the composition being in a lipophilic carrier.

Conclusion

No claims allowed. All claims rejected. No claims objected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Supervisory Patent Examiner, Art Unit 1611